LETTERS TO THE EDITOR

Scope
Heart welcomes letters commenting on papers published in the journal in the previous six months. Topics not related to papers published earlier in the journal may be introduced as a letter: letters reporting original data may be sent for peer review.

Presentation
Letters should be:
- initially submitted by fax +44 171 388 0323 or e-mail 100536.2733@compuserve.com (where practicable). Always follow this up by posting the paper copy to us
- not more than 600 words and six references in length
- typed in double spacing (fax copies and paper copy only)
- signed by all authors.

They may contain short tables or a small figure.

Pathophysiology and time course of silent myocardial ischaemia during mental stress

SIR,—Most patients in the study by Legault *et al* did not develop anginal chest pain when the ejection fraction decreased during periods of mental stress.[1] The authors, however, did not comment on this finding. The precise mechanism responsible for the lack of symptoms associated with the ischaemic episode induced by mental stress in the laboratory has not been explained. It has been postulated that an alteration in the pain threshold might account for the silent nature of ischaemic episodes during periods of mental stress. However, there is little support for this hypothesis in published reports.

The major drawback of the study by Legault *et al* was the lack of correlation between ischaemia induced during mental stress in the laboratory and evaluations made by ambulatory electrocardiographic monitoring performed for 24–48 h in the patient's own environment.[1] A recent study has provided clinically meaningful information on this aspect. Gottdiener *et al* evaluated the relation between myocardial ischaemia induced by mental stress and the functional severity of ischaemia during exercise stress testing and triggers of ischaemia during daily life. They showed that in patients with confirmed coronary artery disease, the induction of myocardial ischaemia by mental stress was predictive of an increased risk of myocardial ischaemia during routine daily life. However, most ischaemic episodes during daily life occurred at times of low mental stress. These results suggest that findings observed during psychological stress testing in the laboratory might not correlate well with the magnitude of stress perceived by patients during daily life.

Legault *et al* failed to prove the clinical significance and prognostic importance of their findings. Information about the clinical impact of ischaemia induced during mental stress in the laboratory has been lacking because most studies, including the present one, have not correlated their findings with the risk of ischaemia encountered during daily life or provided longitudinal follow up data on the patients evaluated. Clearly, more work is needed in this area especially to document the significance of findings observed in the laboratory by correlation with evaluations made in the patients' own environments.

The dynamic decrease in coronary supply induced by mental stress may have been secondary to an increase in α adrenergic activity produced by mental stress.[3] This hypothesis carries important therapeutic implications. Treatment with α adrenergic blocking agents alone or in combination with β receptor blocking agents might be the most effective regimen. However, if coronary vasoconstriction seems to be playing a dominant role, it is possible that treatment with calcium channel blockers would be appropriate. At present, there is little if any information available to establish the superiority of one anti-ischaemic regimen over another as a treatment for myocardial ischaemia induced by mental stress.

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1 Legault SE, Freeman MR, Langer A, Armstrong PW. Pathophysiology and time course of silent myocardial ischaemia during mental stress: clinical, anatomical, and physiological correlates. *Br Heart J* 1995;73: 242–9.
2 Gottdiener J, Krantz D, Howell R, Hecht G, Klein J, Falconer J, *et al.* Induction of silent myocardial ischemia with mental stress testing: relation to the triggers of ischemia during daily life activities and ischemic functional severity. *J Am Coll Cardiol* 1994; 24:1645–51.
3 Ahlawat SK. Mental stress and myocardial ischemia. *J Assoc Phys India* 1993;41:769.

This letter was shown to the authors, one of whom replies as follows:

SIR,—As Dr Ahlawat correctly points out, the mechanisms responsible for pain during myocardial ischaemia are not fully elucidated. Our finding that ischaemia induced by mental stress was usually painless is consistent with the findings of Rozanski *et al* and Gottdiener *et al.*[1 2] The pathophysiology of ischaemia may be important in causing symptoms; in particular, ischaemia may be more likely to be asymptomatic when increases in heart rate or blood pressure are modest. We[3] and others have shown that the pain threshold is higher in patients with silent rather than symptomatic myocardial ischaemia.

The aim of our study was to gain insight into the pathophysiology of ischaemia induced by mental stress. We did not set out to assess possible correlations between ischaemia induced by mental stress in the laboratory and during daily life. However, in another study we found that the ischaemic response to mental stress predicted the frequency of ambulatory ischaemia independently of the left ventricular response to exercise.[4] Moreover, patients with ischaemia induced by mental stress had more frequent episodes and longer total duration of ambulatory ischaemia. These findings suggest that the ischaemic response to mental stress may be a clinically relevant finding.

Gottdiener *et al* found that patients with ischaemia induced by mental stress had more ischaemia (detected by ambulatory monitoring) during sedentary activities but did not differ in terms of total number or duration of episodes of ambulatory ischaemia.[2] Only 26% of episodes of "sedentary ischaemia" during ambulatory monitoring were accompanied by high mental or emotional arousal. One interpretation of these findings is that vulnerability to ischaemia induced by mental stress in the laboratory may be a marker for higher prevalence of "sedentary" ambulatory ischaemia—that is, ischaemia induced in the laboratory by mental stress may be an index for vulnerability to ischaemia that is mediated by factors other than increased demand in myocardial oxygen supply. In daily life, the aetiology of "sedentary ischaemia" may be multifactorial including, but not limited to, mental stress triggers. For example use of caffeine or nicotine and the diurnal variation and catecholamines, cortisol, and autonomic nervous system arousal may be other factors in the aetiology of "sedentary ischaemia". In addition, activities that were regarded as sedentary—such as reading, watching television, talking, or performing clerical work—may result in similar levels of mental stress as Gottdiener *et al*'s laboratory mental arithmetic task.

We agree that a longitudinal study to examine the clinical significance and prognostic importance of ischaemia induced by mental stress is clearly desirable but this was beyond the scope of the present study. However, a more detailed understanding of the pathophysiology of ischaemia induced by mental stress, as provided by this study, may have important therapeutic implications. A treatment study of pharmacological and non-pharmacological approaches to treatment would be of interest.

Novel and clinically relevant findings of our study include: (*a*) data on the time course and left ventricular volume changes that accompany myocardial ischaemia induced by mental stress; (*b*) the trend for more severe anatomical disease in patients with ischaemia induced by mental stress, which became statistically significant in the subgroup of patients not on β blockers; (*c*) evidence that β blockers may protect against speech induced ischaemia. The latter finding is consistent with a study by Bairey *et al* which showed that β blockers may be effective in suppressing ischaemia caused by mental stress.[5]

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1 Rosanski A, Bairey CN, Krantz DS, *et al.* Mental stress and the induction of silent myocardial ischemia in patients with coronary artery disease. *N Engl J Med* 1978; 318:1005–12.
2 Gottdiener J, Krantz DS, Howell BA, *et al.* Induction of silent myocardial ischemia with mental stress testing: relation to the triggers of ischemia during daily life activities and to ischemic functional severity. *J Am Coll Cardiol* 1994;24:1645–51.
3 Langer A, O'Connor P. Central modulation of pain perception in patients with silent myocardial ischemia. *Am J Cardiol* 1994; 74:182–3.
4 Legault S, Langer A, Armstrong P, *et al.* Usefulness of ischemic response to mental stress in predicting silent myocardial ischemia during ambulatory monitoring. *Am Coll Cardiol* 1995;75:1007–11.
5 Bairey CN, Yang L, Berman DS, *et al.* Comparison of physiologic ejection fraction responses to activity in daily living: implication for clinical testing. *J Am Coll Cardiol* 1990;16:847–54.